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ABSTRACT OF THESIS

COMPARISON OF MORNING WITH AFTERNOON NITROGEN

ELIMINATION IN RESTING SUBJECTS BREATHING 100% OXYGEN

The purpose of this study was to compare morning with afternoon nitrogen elimination rates in subjects breathing 100% oxygen. Less nitrogen elimination during the morning could possibly account for the higher incidence of altitude-induced decompression sickness reported during the morning.

Eighteen male and two female subjects between the ages of 18 and 40 years breathed 100% oxygen for 25 minutes on two occasions, once in the morning, approximately one hour after they arose from bed, and once in the afternoon, approximately eight hours after arising. The denitrogenation sessions were at least 12 hours apart. Subjects were non-smokers, in good health, and met U.S. Air Force body weight standards. Their physical activity, exposure to heat and cold stress, diet, and ingestion of alcohol and caffeine were restricted prior to each experiment.

Exhaled gases were collected in large rubber collecting bags contained (jacketed) within another bag through which oxygen flowed to minimize the inward diffusion of atmospheric nitrogen. After each experiment, the percentage of nitrogen in the collecting bags was measured using a Perkin Elmer MGA-1100 Medical Gas Analyzer. The volume of collected gas was measured using an Alpha Technologies Ventilation Measurement Module. During the first 60 to 90 seconds of

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No difference was noted between the volume of nitrogen eliminated in the morning (190.1 + 82.5 ml, STPD) or afternoon (176.5 + 47.9 ml, STPD) sessions. However, significant correlations were noted between nitrogen elimination and physiological parameters associated with stress (e.g., increased heart rate and increased carbon dioxide elimination) implying that psychological and metabolic factors may influence the rate of nitrogen elimination. The subject's height and the volume of nitrogen exhaled during the lung rinse (pulmonary nitrogen) were also positively correlated with systemic nitrogen elimination. Female gender and increasing age were negatively correlated with nitrogen elimination. A significant, but small, increase in body temperature, as measured in the auditory canal, was noted in the afternoon.

These data suggest that there is no diurnal variation in the effectiveness of breathing 100% oxygen as a means of denitrogenation. The increased incidence of DCS during the morning hours must therefore be due to other factors.

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Summer, 1988

THESIS

COMPARISON OF MORNING WITH AFTERNOON NITROGEN ELIMINATION IN RESTING SUBJECTS BREATHING 100% OXYGEN

Submitted by

Grant A. Brown

Department of Physiology

In partial fulfillment of the requirements

for the Degree of Master of Science

Colorado State University

Fort Collins, Colorado

Summer, 1988

COLORADO STATE UNIVERSITY

APRIL 29, 1988

WE HEREBY RECOMMEND THAT THE THESIS PREPARED UNDER OUR SUPERVISION BY GRANT A. BROWN ENTITLED COMPARISON OF MORNING WITH AFTERNOON NITROGEN ELIMINATION IN RESTING SUBJECTS BREATHING 100% OXYGEN BE ACCEPTED AS FULFILLING IN PART REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE.

Committee on Graduate Work

Jeffrey A. Glen

C W Miller

Alan Tucker

Adviser

C W Miller

Department Head

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CHAPTER I

INTRODUCTION

The possibility of decompression sickness (DCS) in aviators was predicted as early as 1917 (30). By the 1930's when altitude records were being set above 50,000 feet by aircraft and balloon ascent, altitude DCS was indeed a common occurrence (30). During World War II this affliction was a major problem for trainees in hypobaric chambers and, although reporting has been fragmentary, over 17,000 cases of altitude-induced DCS have been reported (8,19,23,42,43,46-48). In spite of improved aircraft pressurization systems, more stringent physical requirements for aircrew members, and other protective measures, such as denitrogenation before exposure to altitude and not flying after scuba diving, DCS still occurs (8,19,23,42,43,46-48). Recent studies of technicians working as inside observers in hypobaric training chambers have revealed an incidence rate of DCS as high as 6.16 per 1000 exposures. When only "flights" to a simulated altitude of 43,000 feet were considered, the rate of DCS was 26.1 per 1000 exposures (46). DCS is also possible when flying an unpressurized aircraft above 18,000 feet, or having a loss of cabin pressurization above this altitude (48). Pilots of high altitude reconaissance aircraft are at risk of developing DCS (42) as are astronauts performing extra-vehicular activity (35).

Although the precise etiology of DCS is not known, the "bubble theory" is most widely accepted (9,17,21,30,41) and nitrogen is the

primary gas involved (30,36,59). Under normal conditions, the amount of dissolved nitrogen in the body is in equilibrium with the partial pressure of nitrogen in the alveoli of the lungs. Decreasing the partial pressure of nitrogen in the alveoli, as occurs when breathing 100% oxygen, results in gradual diffusion of nitrogen out of the body. Unfortunately, if a significant amount of dissolved nitrogen remains in body fluids or tissue during a rapid reduction of ambient pressure, the body's ability to hold the nitrogen in solution is exceeded, resulting in bubble formation (2,36,59).

Dissection, X-rays, microscopy, and Doppler studies have demonstrated bubbles intracellularly and in veins, arteries, lymphatic vessels, and tissue spaces (9,30). Once formed, these bubbles may remain asymptomatic (9) or they may cause one or more types of DCS. By far the most common form of DCS is bends (11,12,20,48), manifested by pain or discomfort in or around skeletal joints. More serious forms of DCS include chokes and neurological DCS caused by gas emboli or bubble formation within the cardio-respiratory system or central nervous system. Chokes and neurological DCS have caused at least 17 altitude DCS fatalities (22). Skin bends is a minor problem but may precede more serious forms of DCS (30).

The main precipitating factors for DCS are the extent of decompression (17,27,31,32,46) and duration of exposure to the reduced pressure (2,17,30). Individual factors increasing susceptibility to DCS include obesity (1,11,17,30,45), increased age (17,30,32,45,47), exercise during exposure to altitude (1,21,26,30, 32,43,49), and reduced body temperature (28,49). Environmental factors increasing susceptibility include cold temperature (30), flying

after scuba diving (3,6), and repeated exposure over a short period of time (30). An increased incidence has also been noted in the morning when compared to afternoon exposures (17,22,29,42,43,52). No definite correlation has been detected between DCS and physical fitness, diet, hypoxia, or fluid intake (17,30,37). Likewise, race, gender, and psychological factors have shown no definite correlation (30,35).

The fundamental prophylaxis against DCS for individuals anticipating exposure to reduced pressure in hypobaric chambers, aircraft, or spacesuit is denitrogenation. This is accomplished by breathing oxygen immediately before exposure (17,30). Several studies have proven the effectiveness of oxygen prebreathing (18,25,26,32, 43,44,56); furthermore, the degree of protection offered by oxygen prebreathing is related to the time spent in this denitrogenation period (18,22,42,56).

The purpose of this study was to determine whether or not there is a significant diurnal variation in the amount of nitrogen offloaded during a controlled denitrogenation period. Such a variation could help explain the increased incidence of DCS in the morning when compared to afternoon exposures.

CHAPTER II

REVIEW OF THE LITERATURE

Historical Perspective of Altitude DCS Research

During World War II there was a great proliferation of DCS research due to the increasingly high altitudes at which unpressurized aircraft operated. Germany introduced pressurized reconaissance aircraft over Africa capable of flying at 42,000 feet. Lovelace, as cited by Tobias (55), noted that two of the first three British flyers who managed to climb to this altitude and shoot down these aircraft with their unpressurized Spitfire fighters suffered almost incapacitating bends. Also, nearly 25% of bomber crew members questioned had developed bends during their combat missions (55).

Practically all DCS research was conducted in hypobaric training chambers. Analysis of 9,500 cases of DCS occurring at one of many training facilities, by Motley et al. (43), is indicative of the extent of the problem. The findings of these studies are especially significant because of the large number of subjects involved and the fact that such hazardous, occasionally fatal, studies will understandably never be repeated with human subjects. Pertinent findings from the early era of research, along with more recent data relevant to this current study is presented in the following sections.

Variation of Incidence of DCS with Time of Day

Several investigators have noted a decreasing incidence of DCS later in the day. Guest (29) reported a 30% DCS rate among 2,693 altitude chamber trainees between 7:00 a.m. and noon. The incidence rate dropped to 15.4% among 2,593 trainees between 1:00 p.m. and 6:00 p.m. Altitude exposure for both groups was 38,000 feet for 3 hours. Thompson et al. (52) noted a 41% DCS incidence in 2076 men participating in chamber flights to 35,000 feet between 9 a.m. and noon. This incidence rate dropped to 29% among 1558 men taking the flight between 1 p.m. and 4 p.m. Motley et al. (43) found a 17.9% bends rate during the 6 a.m. to 10 a.m. training period with gradual reduction to 11.6% during the 7:30 p.m. to 10:30 p.m. training period. Fryer (22) noted a similar relationship. Meader (42), reporting on DCS occurring in high altitude WU-2 weather reconaissance aircraft, also found a disproportionate number of bends cases in the morning.

Prevention of DCS by Denitrogenation

Prebreathing oxygen before exposure to altitude has been used for several years to protect against DCS and this procedure's effectiveness has been confirmed by many studies. Meader's (42) study showed a 66% reduction in bends among WU-2 pilots who prebreathed oxygen for 50 to 60 minutes when compared to pilots who prebreathed for 30 to 40 minutes.

Controlled studies by Gray et al. (26) evaluated aviation cadets exposed, at rest, to a simulated altitude of 38,000 feet for 2 hours. Prebreathing oxygen for 15 minutes provided a 52% reduction in severe bends and chokes as compared to controls. Extending the prebreathing time to 45 minutes reduced the incidence rate by 86%.

Motley et al. (43) noted a reduction in bends incidence from 10.6% to 7.3% when subjects breathed 100% oxygen, rather than an oxygen enriched air mixture, during ascent to 30,000 feet. This flight profile consisted of ascent at 2,000 feet per minute to 30,000 feet, 60 minutes at 30,000 feet, and 15 minutes at 38,000 feet. Inside observers who prebreathed oxygen for 45 minutes had a bends rate of only 2%.

Henry et al. (33) studied the incidence of incapacitating bends, precipitated by mild exercise for 90 minutes at a simulated altitude of 35,000 feet. Controls suffered a 52% incidence rate, subjects who prebreathed oxygen for 1 hour had an 18.3% incidence. Henry et al. also stated that there was a marked reduction in effectiveness of denitrogenation in the morning when compared to afternoon and recommended that twice as much denitrogenation time be allowed before morning flights.

<u>Factors Effecting Denitrogenation Rate</u>

The following factors have demonstrated an influence on denitrogenation rates.

Exercise: Behnke and Willmon (10) noted a 39% increase in the amount of nitrogen exhaled while pedalling an exercise bike for 30 minutes when compared with sitting on the bike, at rest, for 30 minutes.

Diet: Controlled studies by Cissik et al. (16) suggested that increasing the quantity of protein in a meal before evaluation increased the amount of nitrogen exhaled by the subject. Although this was refuted by Wilmore et al. (58) and others, specific dynamic action (24) and redistribution of blood flow with increased blood flow to the

gastrointestinal tract (24) could also conceivably influence denitrogenation rates

Water Immersion: Experiments conducted by Balldin and Lundgren (7) showed a 40% increase in the amount of nitrogen offloaded over a 30-minute period of oxygen breathing by subjects immersed in neutral (35°C) water with the head above water. This was compared to oxygen breathing in the sitting position, in dry conditions.

Temperature: Balldin and Lundgren (7) also showed that increasing the water temperature in the previous experiment to 37°C increased the quantity of nitrogen offloaded by another 9%. Bove et al. (14), studying the rate of inert gas elimination from rabbits, showed that inert gas washout varied significantly from normal during heat and cold stress.

Carbon Dioxide Inhalation: Margaria and Sendroy (40) had subjects breathe various oxygen/carbon dioxide mixtures and measured the amount of nitrogen exhaled. Breathing 5% CO_2/95% O_2 for 30 minutes, after exposure to slightly more than 2 atmospheres while breathing air for 4 hours, increased nitrogen offloading by 20%. Breathing 3% CO_2 caused no increase nor did increased pulmonary ventilation. The latter finding is also in agreement with Stevens et al. (51) who had subjects hyperventilate vigorously while breathing oxygen. The amount of nitrogen exhaled during hyperventilation was the same as when the subjects breathed normally.

Time of Day: Stevens et al. (51) compared the amount of nitrogen exhaled during a specified length of time during morning and afternoon sessions. They found no difference; however, their subjects were controlled in only two respects: (1) they breathed air at ground

level for 8 hours preceding the test, and (2) the subjects emptied their bladder before denitrogenation. Nearly one-half of the subjects were smokers and there was no control of diet, exercise, or room temperature (which varied from 23° to 31°C) during the experiments. Also, they used a rebreathing system that allowed subjects to inhale up to 7% carbon dioxide on a few occasions. Any of these factors could have had a negative impact on the accuracy of their results.

Statement of Hypothesis

Based on the previous studies cited in the review of literature, we tested the hypothesis that subjects breathing 100% oxygen will denitrogenate at a slower rate during the morning when compared with denitrogenation during the afternoon. The primary objective of this study was to determine diurnal variations in the effectiveness of breathing 100% oxygen as a means of denitrogenating subjects anticipating exposure to pressure reductions capable of causing altitude-induced decompression sickness.

CHAPTER III

PROCEDURES

Before proceeding with this study, approval was obtained from the Colorado State University Human Research Committee. Each subject was informed of the study's procedures, risks, and benefits prior to giving his or her informed consent, and they were informed that they could withdraw from the study at any time.

Subject Selection

A total of 22 healthy male (20) and female (2) volunteer subjects between the ages of 18 and 40 participated in this study. All subjects were Colorado State University students and faculty. They were non-smokers and met U.S. Air Force body weight standards.

Treatment

Each subject breathed oxygen (minimum purity 99.8%) for 25 minutes on two occasions. One of these denitrogenation sessions took place in the morning, approximately one hour after the subject arose from bed. The other session was conducted in the afternoon, approximately 8 hours after arising. The sessions were at least 12 hours apart. One-half of the subjects were evaluated first in the afternoon, the other one-half were evaluated first in the morning. As they volunteered, they were consecutively assigned morning or afternoon sessions as their first evaluation, their schedule permitting.

Research Methods

Rest Period: Prior to denitrogenation, the subject rested, while sitting, for 20 minutes. The subject's heart rate and blood pressure were measured at the beginning and end of the denitrogenation sessions. The subject's body temperature was measured using the left auditory canal. A small (0.08 inch diameter) flexible thermocouple probe was inserted approximately 1.5 cm into the ear canal. To avoid pain or trauma to the ear canal or tympanic membrane, the portion of the probe inserted into the ear canal was contained within a soft, sponge rubber ear plug. A cone-shaped opening was cut in the end of the ear plug encircling the sensor tip of the thermocouple probe. This exposed the sensor to the air in the ear canal yet the sensor did not extend past the end of the ear plug. A clean, new ear plug was used for each subject. The thermocouple was connected to a telethermometer to display and record the subject's temperature.

Denitrogenation Procedure: Partial denitrogenation was accomplished by having the subject breathe 100% oxygen for 25 minutes. At the end of the rest period, the subject attached a noseclip, exhaled maximally, and inserted the mouthpiece of the breathing system. During the first 60 to 90 seconds of oxygen breathing, the subject performed 6 vital capacity breaths to eliminate "pulmonary" nitrogen. A three-way valve was connected to the exhalation portion of the respiratory valve. This allowed pulmonary gases to be diverted into a separate collection bag during the lung rinse (pulmonary nitrogen). At the end of the lung rinse, the subject held his or her breath while the valve was repositioned. Breathing during the next 25 minutes was at a normal

rate and depth and nitrogen exhaled during this time period was measured as "systemic" nitrogen.

Breathing System: The subject breathed oxygen from a high pressure oxygen cylinder connected to a U.S. Air Force A-14 demand regulator. Oxygen was delivered from the regulator, through a respiratory hose, to a Hans-Rudolph series 2700 breathing valve, to which the mouthpiece was attached. Exhaled gases passed through the exhalation portion of the Hans-Rudolph valve, through another length of respiratory hose, and into two large rubber collection bags. One-way valves in the Hans-Rudolph valve prevented backward movement of gas within the system. The regulator, respiratory hoses, respiratory and 3-way valves, and collection bags for systemic nitrogen were contained (jacketed) within a plastic and rubber system through which oxygen flowed during the experiments. This minimized the possibility of nitrogen diffusion from the atmosphere into the collected gases.

Immediately after each experiment, the volume of accumulated, exhaled gas was measured with an Alpha Technologies Ventilation Measurement Module (VMM) and the percentage of nitrogen was measured with a Perkin-Elmer MGA-1100 Medical Gas Analyzer (mass spectrometer). Multiplying these figures, after correcting for temperature and pressure, provided the total amount of nitrogen (STPD) exhaled by the individual.

Complete calibration of the mass spectrometer was performed weekly and its proper sensitivity to nitrogen was determined before each experiment. The VMM calibration was checked periodically using a 3 liter Collins Super-Syringe. Also, a premeasured volume of 30 liters

of air was passed through the VMM from the collection bags to ensure accurate measurements using the employed experimental methods.

Subject Restrictions

Diet: Subjects fasted, except for water, for at least 5 hours prior to the denitrogenation sessions. They received a low protein, low fat snack at the beginning of the rest period. Subjects were also requested to refrain from alcohol or caffeine ingestion for 8 hours prior to evaluation.

Exercise: Subjects were requested to refrain from strenuous activity for the 12 hours preceding their sessions and traveled to the session by automobile.

Temperature Restrictions and Controls: The same type of clothing was worn by the subjects during each session and they refrained from bathing, showering, swimming, or being exposed to heat or cold stresses for 6 hours prior to the sessions. Both evaluations for each female subject were conducted during the same phase of her menstrual cycle. This avoided a possible influence by the slight rise in body temperature after ovulation. The temperature in the testing room was maintained at $25 \pm 0.5^{o}C$ for both the morning and afternoon sessions.

Additional Data Collected

The total volume of gas exhaled during the lung rinse and denitrogenation was measured and corrected to STPD. Carbon dioxide exhaled during denitrogenation was also measured.

Data Analysis

Statistical analysis was accomplished using the Colorado State University Cyber mainframe computer with the Statistical Package for the Social Sciences - Expanded (SPSS-X). An analysis of covariance

(ANOCOVA) was performed to compare the difference in systemic nitrogen by time of day (AM vs PM) after significant covariates were determined by stepwise multiple regression. Paired t-tests were performed to detect significant differences in morning and afternoon physiological measurements. A significance level of $P<0.05$ was established *a priori*.

CHAPTER IV

RESULTS

Twenty-two subjects participated in the study but data from two male subjects were eliminated. One participant was unable to maintain an air-tight seal around the mouthpiece, the other subject's data were not used because of his consistently high mean blood pressure readings, averaging 108 mm Hg. Subject characteristics including gender, age, height, and weight, of the remaining 20 subjects are listed in Table 1.

There was no difference in the volume of nitrogen eliminated between the morning and afternoon sessions (Table 2). Nitrogen elimination was positively correlated ($p<0.05$) with the volume of pulmonary nitrogen collected ($r=0.422$, $p=0.003$), the volume of systemic carbon dioxide collected ($r=0.402$, $p=0.006$), subject height ($r=0.368$, $p=0.010$), and the subject's heart rate at the beginning of denitrogenation ($r=0.301$, $p=0.029$). Negative correlations included female gender ($r=-0.321$, $p=0.022$), and increasing age ($r=-0.276$, $p=0.043$). The Pearson Correlation Coefficients and p-values for all measured covariates are listed in Table 3.

Stepwise multiple regression identified three covariates as appropriately significant for inclusion in the ANCOVA. These covariates were: (1) the amount of nitrogen exhaled during the lung rinse (PULN2), (2) the heart rate at the start of denitrogenation (HRST), and (3) the amount of carbon dioxide eliminated during denitrogenation

Table 1. Physical characteristics of the subjects

Subject	Gender	Age (years)	Height (cm)	Weight (kg)
1	M	21	172.5	65.8
2	M	23	176.5	80.3
3	M	21	182.9	73.9
4	M	21	177.8	76.7
5	M	22	166.4	60.1
6	M	19	172.7	60.3
7	M	19	182.9	70.3
8	M	22	174.0	70.3
9	M	35	168.9	64.9
10	M	18	185.4	65.1
11	M	32	188.0	80.5
12	M	21	176.5	79.8
13	M	35	176.5	68.0
14	F	24	170.2	59.0
15	M	40	172.7	68.3
16	F	22	167.6	53.5
17	M	29	184.2	75.1
18	M	24	167.6	61.2
19	M	33	168.9	63.5
20	M	24	177.8	70.8
Mean ± SD	18/2(M/F)	25.2 ± 6.3	178.5 ± 6.4	68.4 ± 7.6

Table 2. Systemic nitrogen elimination (ml, STPD) during 25 minutes of oxygen breathing

Subject	AM	PM	Increase or decrease in PM value
1	192.7	166.5*	-26.2
2	146.2*	144.4	- 1.8
3	441.2	237.7*	-203.3
4	166.9	145.2*	-21.7
5	206.5*	193.9	-12.6
6	176.3	199.9*	23.6
7	221.5	229.4*	7.9
8	259.2*	216.3	-42.9
9	114.1*	214.0	99.9
10	306.9*	148.1	-158.0
11	177.6*	178.1	0.5
12	121.1*	127.2	6.1
13	157.7	168.6*	11.1
14	154.3*	136.7	-17.6
15	146.9	179.6*	32.7
16	88.0*	100.0	12.0
17	155.5	163.1*	7.6
18	203.5	161.8*	-41.7
19	90.7	116.0*	25.3
20	275.0*	304.1	29.1
Mean ± SD	190.1 ± 82.5	176.5 ± 47.9	-13.5 ± 65.6

*Indicates subject's first evaluation.

Table 3. Pearson Correlation Coefficients, systemic nitrogen elimination with variable time and covariates

TIME r=-0.1025 p=0.265	SEX r=-0.3207 p=0.022	AGE r=-0.2757 p=0.043	HT r=0.3684 p=0.010	WT r=0.1577 p=0.165
HRST r=0.3010 p=0.029	HREND r=0.1267 p=0.218	MBPST r=0.2160 p=0.090	MBPEND r=0.0132 p=0.468	TEMP r=-0.0147 p=0.464
SYSCO2 r=0.4018 p=0.006	SYSTOT r=0.2240 p=0.082	PULN2 r=0.4220 p=0.003	PUTOT r=-0.2399 p=0.068	

Explanation of Acronyms

HRST - Heart rate at the start of denitrogenation,
HREND - Heart rate at the end of denitrogenation,
MBPST - Mean blood pressure at the start of denitrogenation,
MBPEND - Mean blood pressure at the end of denitrogenation,
TEMP - Ear canal temperature in degrees Celsius,
SYSCO2 - Volume (STPD) of systemic carbon dioxide collected during denitrogenation,
SYSTOT - Total volume (STPD) of gases exhaled during denitrogenation,
PULN2 - Volume (STPD) of nitrogen collected during lung rinse,
PULTOT - Total volume (STPD) exhaled during lung rinse.

(SYSCO2). The correlation relationships of these factors with nitrogen production are plotted in Figures 1, 2, and 3.

The ANCOVA performed to determine the difference in denitrogenation by time (AM vs. PM), including the covariates PULN2, PST, and SYSCO2 revealed no significant difference ($F = .92$).

Two-tailed t-tests were performed to compare morning with afternoon physiological measurements. The only significant difference was an increase in afternoon ear canal temperature (Table 4).

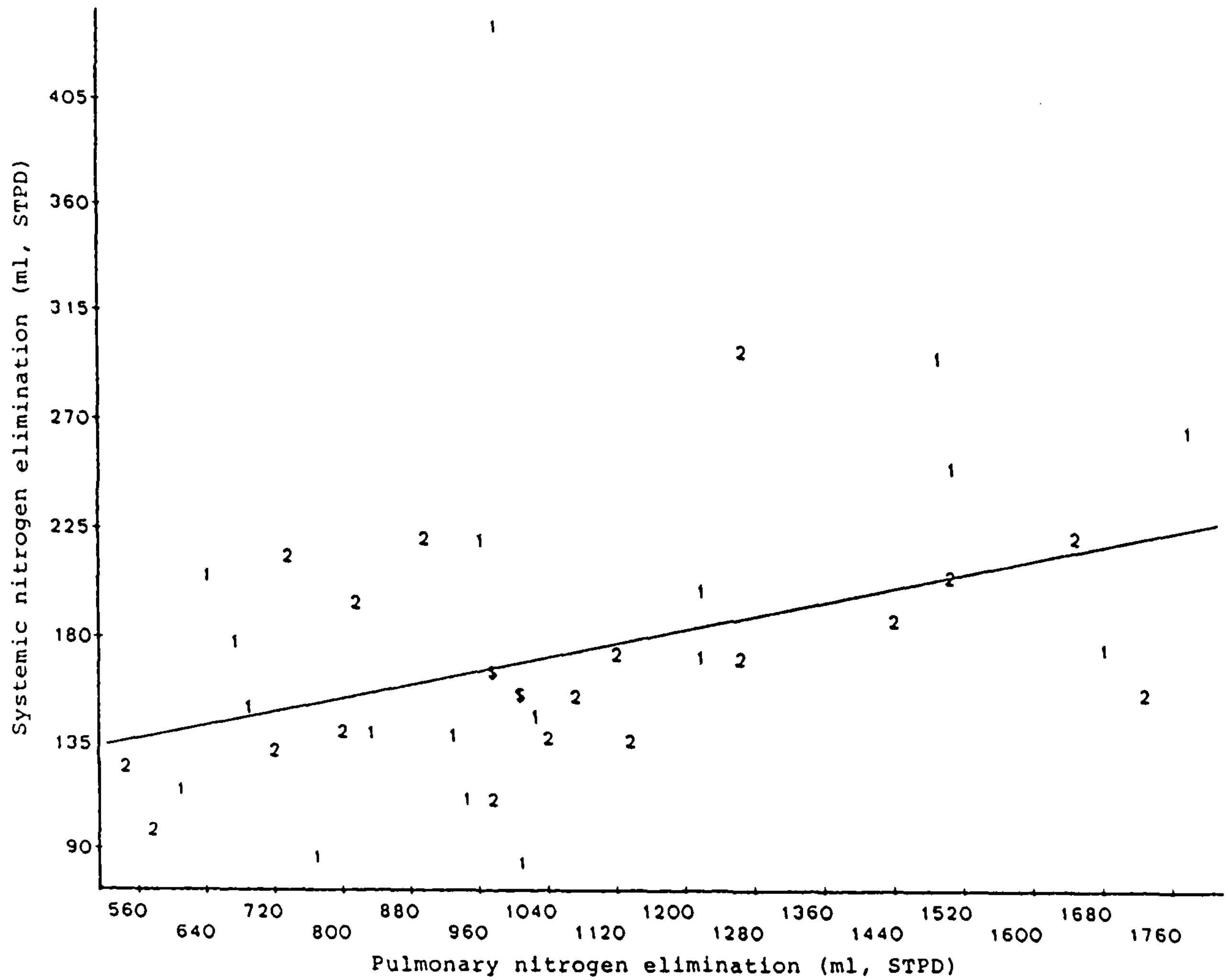

Figure 1. Positive relationship between systemic nitrogen elimination and pulmonary nitrogen elimination. 1 = AM, 2 = PM, $ = multiple occurrences.

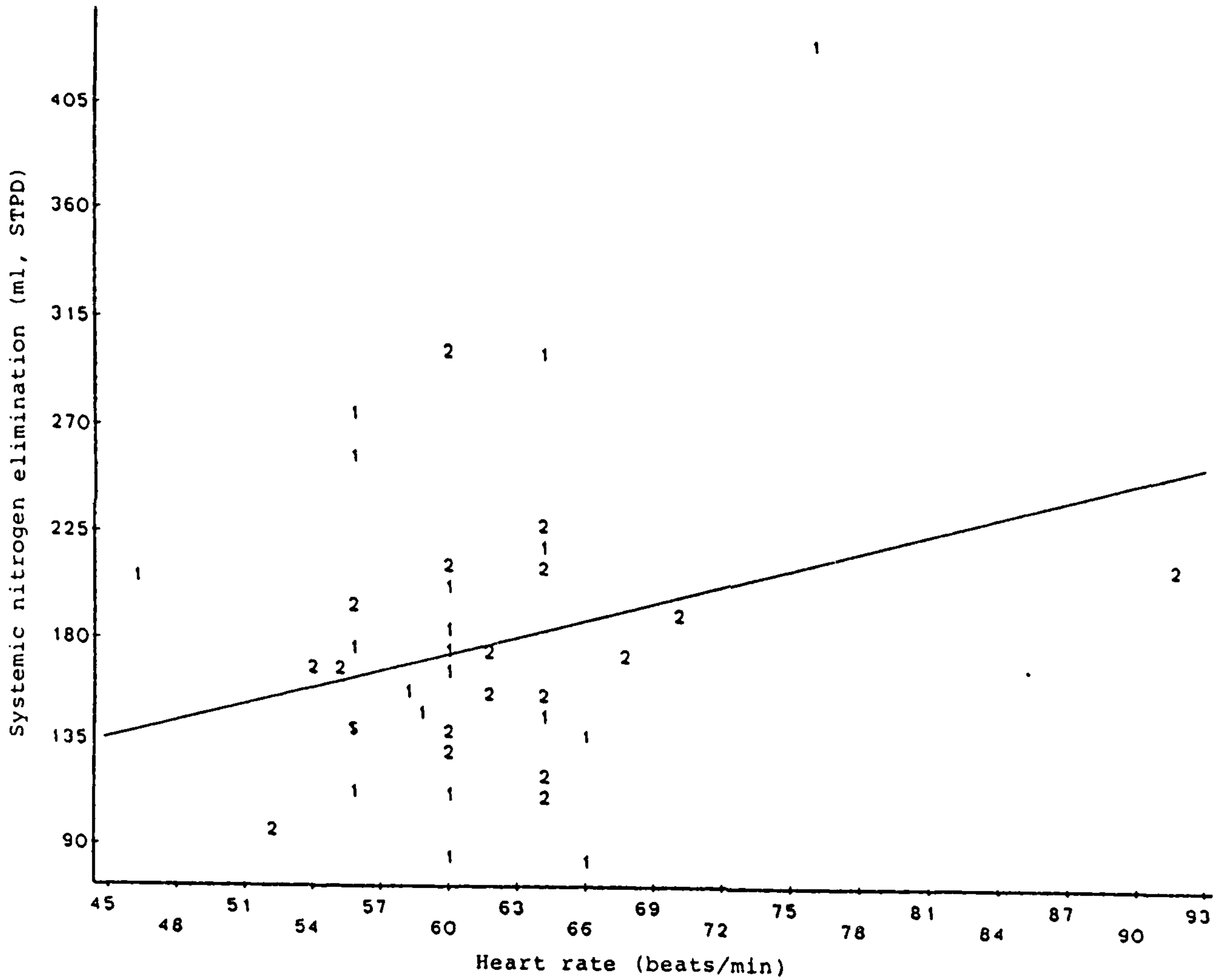

Figure 2. Positive relationship between systemic nitrogen elimination and heart rate at the beginning of denitrogenation. 1 - AM, 2 - PM, $ - multiple occurrences.

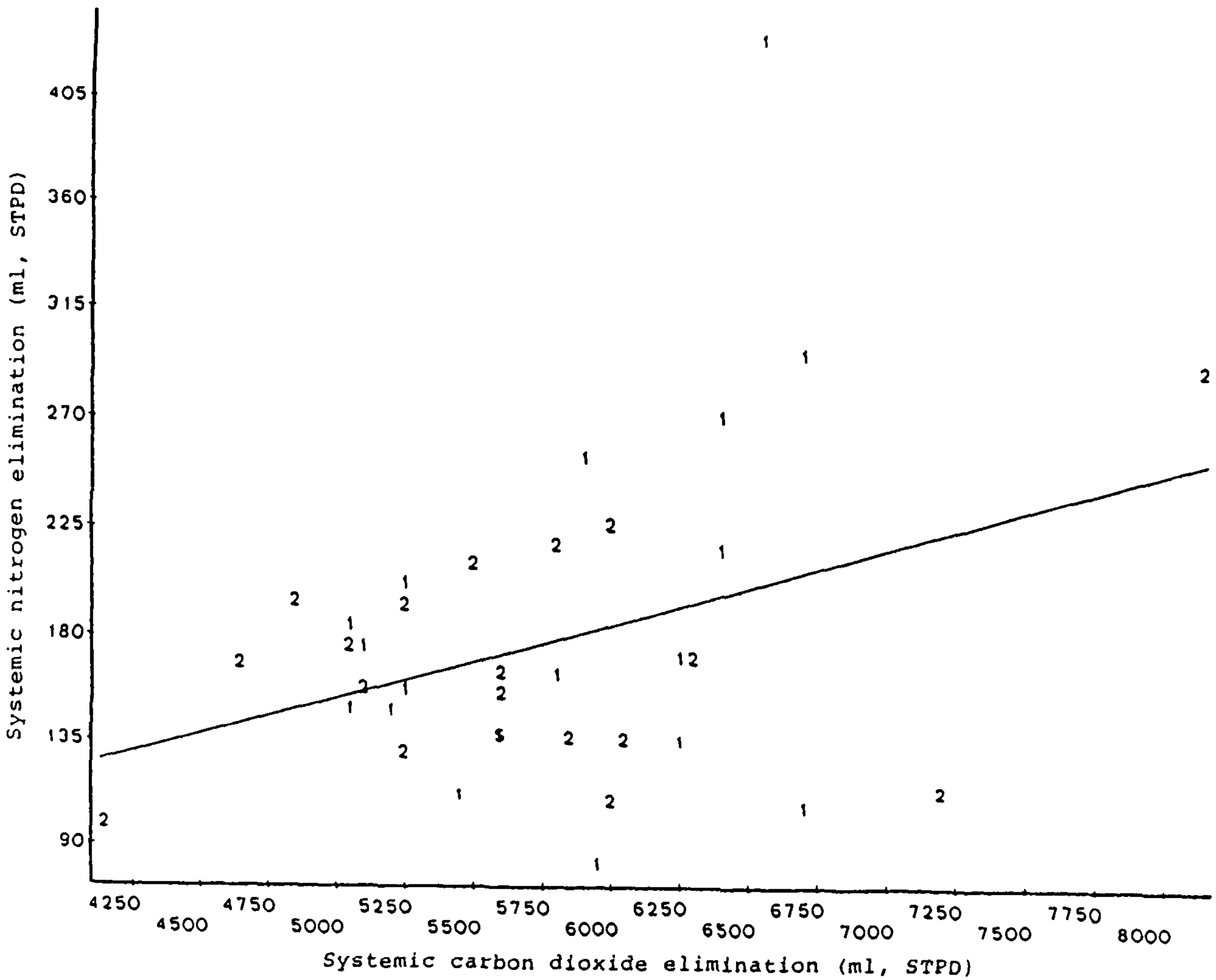

Figure 3. Positive relationship between systemic nitrogen elimination and systemic carbon dioxide elimination. 1 = AM, 2 = PM, $ = multiple occurrences.

Table 4. Comparison of morning with afternoon physiological measurements

Parameter	AM Mean ± SE	PM Mean ± SE	Increase or Decrease in PM value
HRST (beats/min)	60.2 ± 1.3	62.4 ± 1.9	2.2
HREND (beats/min)	62.0 ± 1.5	63.7 ± 1.7	1.7
MBPST (mm Hg)	90.1 ± 1.5	89.8 ± 1.3	-0.35
MBPEND (mm Hg)	90.3 ± 1.6	90.3 ± 1.5	0.05
TEMP (^{o}C)	35.81 ± 0.08	35.97 ± 0.08	0.16*
SYSN2 (ml, STPD)	190.1 ± 18.4	176.5 ± 10.7	-13.5
SYSCO2 (ml, STPD)	5824.2 ± 140.8	5804.9 ± 191.3	-19.3
SYSTOT (ml, STPD)	168211.7 ± 5564.0	171514.0 ± 6093.7	3302.3
PULN2 (ml, STPD)	1045.9 ± 75.8	1062.2 ± 74.7	16.3
PULTOT (ml, STPD)	18447.5 ± 1267.3	17490.2 ± 859.0	-957.3

Explanation of Acronyms

HRST - Heart rate at the start of denitrogenation,
HREND - Heart rate at the end of denitrogenation,
MBPST - Mean blood pressure at the start of denitrogenation,
MBPEND - Mean blood pressure at the end of denitrogenation,
TEMP - Ear canal temperature in degrees Celsius,
SYSN2 - Volume (STPD) of systemic nitrogen collected during denitrogenation,
SYSCO2 - Volume (STPD) of systemic carbon dioxide collected during denitrogenation,
SYSTOT - Total volume (STPD) of gases exhaled during denitrogenation,
PULN2 - Volume (STPD) of nitrogen collected during lung rinse,
PULTOT - Total volume (STPD) exhaled during lung rinse.

*$p<0.05$

CHAPTER V

DISCUSSION

Many findings of this study confirm and support the data comparing morning with afternoon nitrogen elimination published by Stevens et al. (51) who, as previously noted, failed to control several variables that could have had a negative impact on their findings. However, there are also some notable differences. The main finding of both studies was that there is no difference between morning and afternoon nitrogen elimination. Both studies also noted a positive correlation between nitrogen elimination and carbon dioxide elimination ($r=0.43$ in the Stevens et al. study, $r=0.40$ with $p=0.006$ in the present study) and height ($r=0.44$ in the Stevens et al. study, $r=0.37$ with $p=0.01$ in present study). These findings indicate increased metabolism causing increased carbon dioxide production which would in turn cause increased blood flow and nitrogen offloading by the involved tissues. Also, if the lung rinse was not totally effective in clearing all pulmonary nitrogen, the remaining nitrogen would erroneously be measured as systemic nitrogen. This error would be magnified in taller subjects because of their greater residual lung volume. Problems with the lung rinse will be discussed in greater detail later.

The large variation in nitrogen elimination within and between subjects in this study is comparable to variations noted by Stevens et al. (51) and other investigators (6,7,10,13,39). No single cause of these variations has been determined; rather, several factors or

combination of factors seem responsible. For example, as mentioned earlier, if the effectiveness and volume of the lung rinse were not exactly the same with each experiment, any residual nitrogen in the lungs would be measured as systemic nitrogen. Also, any physical activity during the experiment would increase metabolism and increase nitrogen elimination.

Likewise, any factor increasing cardiac output and tissue blood flow would increase nitrogen elimination. Such a change in cardiac output and tissue perfusion could be caused by a generalized stress response exhibited by subjects who were generally anxious about the testing procedure, uncomfortable using the mouthpiece, or experiencing pain from the noseclip. Anxiety and excitement, for example, can increase cardiac output by 50 to 100 percent, primarily mediated by accelerated heart rate (24). Specifically, epinephrine secretion during stressful situations causes increased rate and force of contraction of the heart and dilation of the resistance vessels of skeletal muscle (50). These actions would expedite removal of the large store of nitrogen from skeletal muscle. Epinephrine also causes increased systolic blood pressure and decreased diastolic blood pressure resulting in no change in the mean arterial blood pressure (50). This could explain why nitrogen elimination was significantly correlated with the heart rate at the start of denitrogenation ($r=0.30$, $p=0.029$) but not with the mean blood pressure.

There are several areas of disagreement between the results of the Stevens et al. (51) study and the current study. For example, Stevens et al. noted a positive correlation between nitrogen elimination and body weight. No such correlation was noted in the current study.

Perhaps their conclusion was due to the failure to place a restriction on the degree of fatness of the subjects. One of the female subjects was 163 cm (64 in.) tall and weighed 104.6 kg (232 lbs). Having such a large variation of body fat between subjects would increase the likelihood of correlation between nitrogen elimination and body weight because nitrogen is five times more soluble in fat than in water (57). Subjects in the present study met U. S. Air Force body height and weight standards, thereby reducing intersubject variability.

Another discrepancy is the quantity of nitrogen eliminated by subjects. The subjects in the Stevens et al. study eliminated an average of 346 ml of nitrogen during 20 minutes of oxygen breathing, whereas the subjects participating in the current study eliminated an average of 183 ml of nitrogen during 25 minutes of oxygen breathing. Several factors could be responsible for this discrepancy. For example, the subjects in the Stevens et al. study denitrogenated while reclining, whereas our experiments were conducted in seated subjects. Balldin (4) has demonstrated a 24% increase in nitrogen elimination when subjects denitrogenated while reclining rather than sitting. Also, the Stevens et al. study was conducted at approximately 700 ft above sea level while the present study was conducted at approximately 5,000 ft above sea level. Thus, according to Henry's law, Stevens' subjects began denitrogenation with a greater degree of nitrogen saturation of their tissues. Finally, the failure to control room temperature and carbon dioxide rebreathing in the Stevens et al. study could also have resulted in increased nitrogen elimination.

Significant negative correlations between nitrogen elimination and female gender ($r=-0.32$, $p=0.022$) and age ($r=-0.28$, $p=0.043$) were noted

in the current study. These significant findings can be explained by the presence of other significant variables. For example, collectively, the two female subjects were shorter in height, had less pulmonary nitrogen elimination, lower starting heart rate, and less systemic carbon dioxide elimination than male subjects (Table 5). In other words, female subjects as a group exhibited responses in the most significant covariates that would predict less nitrogen elimination. Table 6 shows data comparing younger subjects with older subjects. The decreased pulmonary diffusing capacity that occurs with increasing age could also contribute to the negative correlation between the rate of nitrogen elimination and age (15). Younger subjects as a group had greater within subject variation in the amount of nitrogen eliminated than older subjects (Table 6). This was probably due to the younger subjects' lack of previous participation in comparable experiments. Only one of the subjects less than age 23 had previously served as a subject. This would make the younger subjects more susceptible to emotional stress and problems with the lung rinse than older subjects, all of whom had previously participated in similar physiological experiments.

Lung Rinse Effects

Accurate systemic nitrogen elimination data cannot be obtained without a precise, standardized method of eliminating nitrogen from the lungs. If this nitrogen is not removed, it will cause artificially high systemic nitrogen elimination measurements. If the lung rinse procedure is too effective, not only will all the pulmonary nitrogen be removed, but systemic nitrogen will diffuse from the blood into the lungs, be exhaled, and measured as pulmonary nitrogen. Unfortunately,

Table 5. Comparison of the most significant physiological measurements, comparing female subjects with male subjects

Parameter	Female (N=2)	Male (N=18)
Height (cm)	168.9 ± 1.8	176.2 ± 6.9
HRST (beats/min)	60.5 ± 6.2	61.3 ± 7.5
PULN2 (ml, STPD)	686.1 ± 86.9	1095.1 ± 359.7
SYSCO2 (ml, STPD)	4874 ± 607.6	5843.6 ± 763.2

Explanation of Acronyms

HRST - Heart rate at the beginning of denitrogenation,

PULN2 - Volume of nitrogen exhaled during lung rinse,

SYSCO2 - Volume of carbon dioxide exhaled during denitrogenation.

Table 6. Comparison of the most significant physiological measurements and within subject nitrogen elimination variation, comparing older subjects with younger subjects

Parameter	Younger Group (N=10)	Older Group (N=10)
Age (years)	18 - 22 years	23 - 40 years
Height (cm)	175.9 ± 6.5	175.1 ± 6.3
HRST (beats/min)	62.0 ± 9.6	60.6 ± 4.8
PULN2 (ml, STPD)	1108.5 ± 391.9	999.7 ± 273.9
SYSCO2 (ml, STPD)	5745.8 ± 798.9	5747.4 ± 696.3
Within Subject Variation, N2 (ml, STPD)	51.4 ± 69.8	26.76 ± 29.1

Explanation of Acronyms

HRST - Heart rate at the beginning of denitrogenation,

PULN2 - Volume of nitrogen exhaled during lung rinse,

SYSCO2 - Volume of carbon dioxide exhaled during denitrogenation.

no standardized lung rinse method has evolved. Examples of published procedures include "a few, rapid maximal respirations in 30 seconds" (13), 5 deep breaths (over an unspecified time period) (3), 5 deep breaths over 30 to 60 seconds (39), 6 maximal breaths in 30 seconds (13), 10 maximal breaths over 30 to 40 seconds (6,7), 10 to 14 maximal breaths over 30 seconds (51), and 18 deep breaths over 3 minutes (10).

The most detailed information concerning lung rinse effectiveness was published by Boothby et al. (13) and Ludin (39). Both studies reported that 6 maximal breaths sometimes washed out pulmonary nitrogen excessively and sometimes inadequately within the same person. This could explain a great deal of variation within and between subjects. For example, a subject who started the lung rinse at residual lung volume, performed maximal vital capacity breaths, and took the maximum allotted time could exhale all pulmonary plus some systemic nitrogen. The opposite extreme would be another subject, or the same subject on a different occasion, who did not completely exhale to residual volume before inserting the mouthpiece and performed less than total vital capacity breaths over a shorter period of time. This would result in incomplete elimination of pulmonary nitrogen which would in turn be reflected as higher systemic nitrogen measurements. Furthermore, if residual volume was not reached before starting the lung rinse in the latter scenario, both pulmonary and systemic measurements would be erroneously increased. This problem would again be magnified in taller subjects who, with larger lung capacities, would have greater potential for variability. This may explain the positive correlation between systemic nitrogen elimination and height and pulmonary nitrogen elimination. Also, taller subjects would have greater pulmonary

diffusing capacity due to their larger lung volume (15) which would tend to increase the rate of nitrogen elimination.

Morning Verses Afternoon Physiological Measurements

The only significant difference between morning and afternoon physiological measurements was a 0.16°C increase in the mean ear canal temperature in the afternoon ($p<.05$). Increased temperature has been associated with increased nitrogen elimination according to Balldin (7). His experiments dealt with immersing subjects for three hours in 32°C, 35°C, and 37°C water which elevated ear canal temperatures 0.6°C during the first 30 minutes of his experiments. There was no correlation between body temperature and nitrogen elimination in the current study, probably because the increase in temperature was so small.

Alternative Theory For Cause of Increased Morning DCS

The emphasis to this point has been on the role of nitrogen, the main constituent of bubbles which must develop before DCS will occur. Once formed, these bubbles may cause adverse mechanical effects within the circulatory system as well as initiate hematological processes that can cascade with devastating consequences. Bubbles not only physically obstruct flow through vessels causing ischemia, they cause platelets to aggregate and release vasoactive substances such as serotonin. These substances cause vasoconstriction and increased capillary permeability allowing increased fluid flow from intravascular to extravascular spaces. Such actions result in further circulatory embarrassment (30).

The extent of platelet involvement is further illustrated by dramatic reductions in platelet counts of up to 50% over 72 hours in human subjects following decompression in a hyperbaric chamber (45).

The term "Nitrogen Bubble-Induced Platelet Aggregation" has been coined due to these interactions (53).

Increased platelet activity in the morning has been demonstrated (44,54) and this increased activity may be related to the increased incidence of myocardial infarction and sudden coronary death between 6 a.m. and noon (54). Since platelets also play such a pivotal role in DCS, their increased morning activity may be partly responsible for the increased incidence of DCS in the morning.

CHAPTER VI

CONCLUSIONS AND RECOMMENDATIONS

A significant difference between morning and afternoon elimination rates of nitrogen from subjects breathing 100% oxygen was not observed in the present study. The correlation of nitrogen elimination with several physiological parameters associated with stress indicates that psychological and metabolic factors may influence denitrogenation. It appears that the increased morning DCS incidence rate is due to a factor other than diurnal variations in the effectiveness of breathing 100% oxygen as a means of denitrogenation. Investigations need to be conducted to evaluate the possibility that diurnal variations in hematological parameters (e.g., increased platelet activity in the morning) may cause the increased incidence of DCS in the morning hours.

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APPENDIX

EXPLANATION OF ACRONYMS

HRST - Heart rate (beats/min) at the start of denitrogenation.

HREND - Heart rate (beats/min) at the end of denitrogenation.

MBPST - Mean blood pressure (mm Hg) at the start of denitrogenation.

MBPEND - Mean blood pressure (mm Hg) at the end of denitrogenation.

TEMP - Ear canal temperature in degrees Celsius.

SYSN2 - Volume (ml, STPD) of systemic nitrogen collected during denitrogenation.

SYSCO2 - Volume (ml, STPD) of systemic carbon dioxide collected during denitrogenation.

SYSTOT - Total volume (ml, STPD) of gases exhaled during denitrogenation.

PULN2 - Volume (ml, STPD) of nitrogen collected during lung rinse.

PULTOT - Total volume (ml, STPD) exhaled during lung rinse.

Appendix Table 1. Raw data collected from all subjects. First set of data presented is from subject's morning experiment, second set is from afternoon experiment. See preceding page for explanation of acronyms and units of measurement.

ID#	HRST	HREND	MBPST	MBPEND	TEMP	SYSN2	SYSCO2	SYSTOT	PULN2	PULTOT
01	60	58	84	85	35.8	192.7	5057	167541	1679	13931
01	54	56	91	87	36.1	166.5	4659	146059	1726	17435
02	56	56	99	97	35.8	146.2	6260	132914	923	14045
02	60	64	96	102	36.2	144.4	5840	131295	798	13585
03	76	74	92	80	36.0	441.2	6547	158702	971	16502
03	64	68	89	93	36.2	237.7	6011	153498	1648	16417
04	60	72	89	87	35.6	166.9	5814	158904	977	17347
04	56	56	80	83	35.2	145.2	5606	164977	1047	14327
05	46	48	85	95	36.2	206.5	----	172065	1208	11763
05	56	60	97	94	35.9	193.9	4872	168589	1437	13572
06	60	68	95	97	36.2	176.3	5117	156050	679	15632
06	70	78	91	89	36.3	199.9	5269	173780	815	11174
07	64	64	93	87	35.6	221.5	6400	199536	967	20016
07	92	86	95	95	36.4	229.4	5800	160408	896	20535
08	56	60	96	95	35.9	259.2	5911	175147	1502	12783
08	60	60	91	87	35.8	216.3	5508	180233	1504	11887
09	56	60	91	89	35.8	114.1	5434	146305	943	17245
09	64	64	87	89	36.1	214.0	5491	178351	742	19177
10	64	60	94	95	35.4	306.9	6700	207391	1484	18908
10	60	64	91	91	35.9	148.1	6062	197399	1135	15972
11	56	54	101	106	35.3	177.6	6237	227610	1218	35873
11	68	60	95	99	35.6	178.1	6315	222609	1270	19855
12	60	64	90	99	36.0	121.1	6705	201746	606	19563
12	64	68	91	93	35.7	127.2	7213	212021	545	17186
13	58	61	98	93	35.7	157.7	5232	178052	1010	20380
13	55	57	100	104	35.9	168.6	5589	183659	969	21260
14	64	62	87	81	35.9	154.3	5199	171480	686	13341
14	60	56	87	84	36.2	136.7	5250	126632	716	12148
15	66	63	94	95	35.4	146.9	5604	136001	839	24197
15	62	68	95	97	35.6	179.6	5054	156942	1121	23166
16	66	72	82	82	36.7	88.0	----	146655	774	22451
16	52	56	85	84	36.6	100.0	4173	145399	568	22804
17	59	62	87	88	36.0	155.5	5029	159251	1028	21949
17	62	61	88	88	36.2	163.1	5084	164865	1009	22137
18	60	64	79	86	----	203.5	5271	147477	633	13042
18	64	64	76	79	----	161.8	5580	215686	1072	18354
19	60	66	77	77	35.4	90.7	5929	149563	1014	24821
19	64	66	83	83	35.9	116.0	6010	149109	969	22085
20	56	52	89	93	35.8	275.0	6391	171843	1779	15162
20	60	62	87	84	35.8	304.1	8148	198769	1258	16728